A Porcine Vascularized Composite Allotransplantation Model For Assessing Early Prognostic Biomarkers Of Rejection

Caitlin Blades[1], Zari Dumanian[1], Paula Arrowsmith[3], Zhaohui Wang[1], Yong Wang[1], Bing Li[1], Kia M. Washington[1], Julia B. Slade[2], Jason Yu[1], Mark Greyson[1], David W. Mathes[1], Evan Farkash[3], Conor L. Evans[2], Nalu Navarro-Alvarez[1], Christene A. Huang[1]

Department of Surgery
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

[1]Department of Surgery, University of Colorado Denver Anschutz Medical Campus, Aurora, CO, USA.
[2]Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA
[3]University of Michigan School of Medicine, Ann Arbor, MI, USA.

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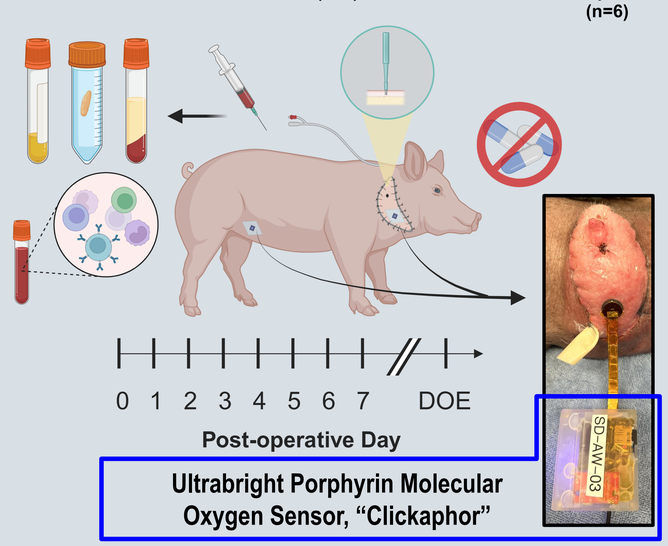
BACKGROUND

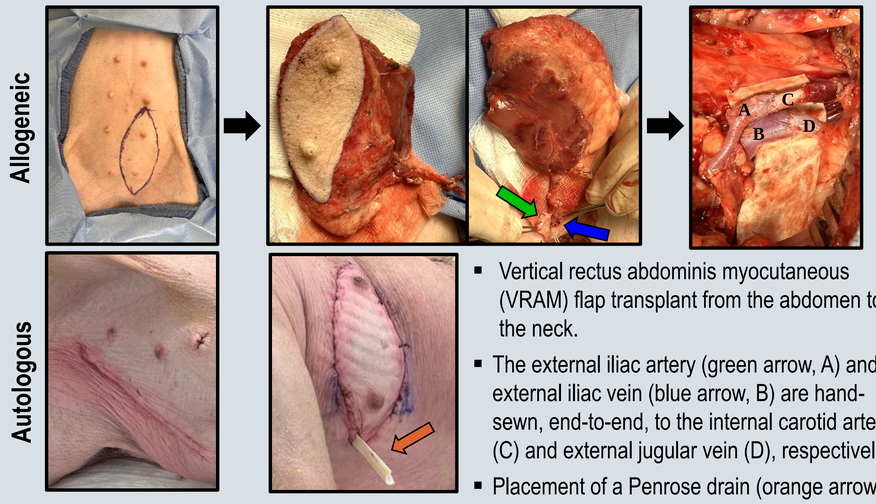
- Vascularized Composite Allotransplantation (VCA) has shown tremendous promise in restoring form and function in patients with large tissue defects
- VCA recipients require immunosuppressive therapy to prevent acute and chronic rejection
- Often at higher levels than for solid organ transplants
- Noninvasive biomarkers of rejection will allow for early detection of signs of rejection and tailored immunosuppression
- Swine models offer skin that is structurally, cellularly, and antigenically similar to humans

METHODOLOGY

- Male and Female 3-4-month-old Yucatan pigs (11.4-18.5 kg) were used as recipients
- Male and Female 7–8-month-old Sinclair pigs (10.9-17.9 kg) were used as donors
- All pigs were non-inbred

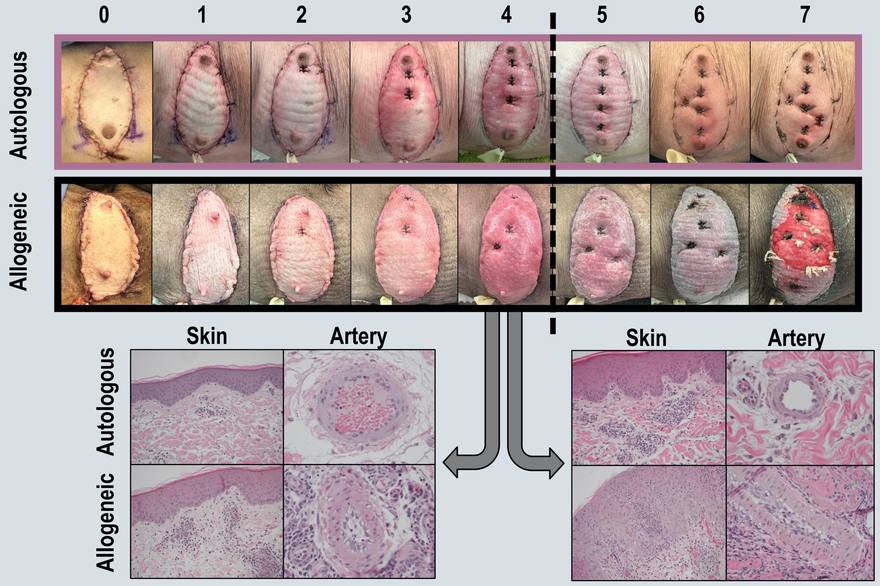


SURGICAL MODEL

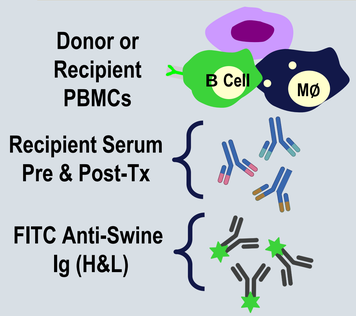


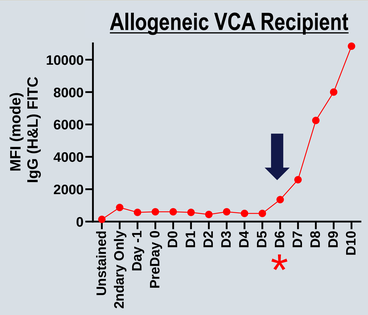
- Vertical rectus abdominis myocutaneous (VRAM) flap transplant from the abdomen to the neck.
- The external iliac artery (green arrow, A) and external iliac vein (blue arrow, B) are hand-sewn, end-to-end, to the internal carotid artery (C) and external jugular vein (D), respectively.
- Placement of a Penrose drain (orange arrow).

RESULTS: GRADE 3 REJECTION IN ALLOGRAFTS BY POD4



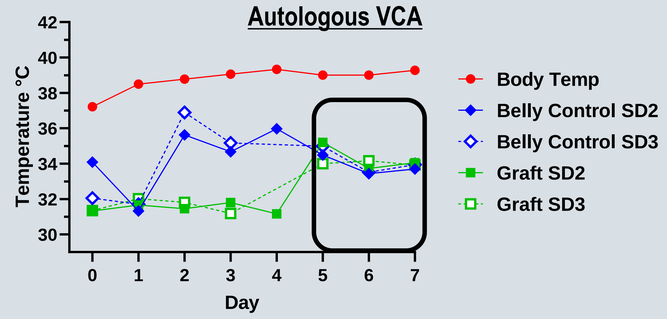
FLOW CYTOMETRY: DONOR SPECIFIC ANTIBODIES (DSAs) ON POD6

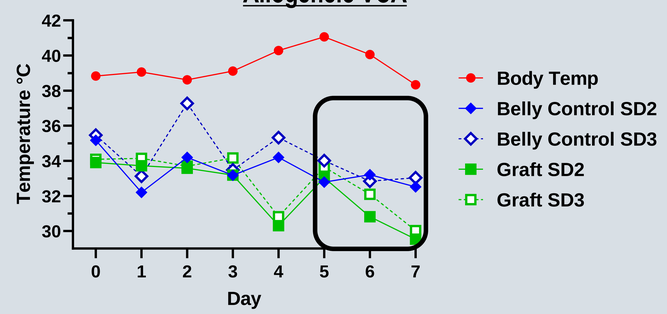




POD6:
DSAs Detected & Graft Biopsy No Longer Bled

TRANSCUTANEOUS TEMPERATURE DECREASE PARALLELS ALLOGENIC VCA REJECTION





CONCLUSIONS

- We have successfully validated a reproducible allogeneic and autologous porcine VCA model
- Allogeneic flaps rejected early in the setting of no immunosuppression
- Graft temperatures correlated well with graft status
- Galectin-3 levels and transcutaneous tissue oxygen levels are currently being analyzed
- Next cohort will be given immunosuppressive therapy until the graft heals, to better assess biomarkers specific for rejection
- Future studies to analyze biomarkers include transcriptomic, proteomic, and metabolomic analyses

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.